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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,808	11/14/2003	Dave S.B. Hoon	89212.0014	4483

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
12/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,808	HOON ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10 and 31-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 10, 31-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Claims 1-7, 10, and 31-35 are pending.

Claims 1, 34, and 35 have been amended by Applicant.

Claims 1-7, 10, and 31-35 are currently under examination.

Rejections Withdrawn

The rejection under 35 U.S.C. 112, second paragraph, is withdrawn.

The rejection under 35 U.S.C. 112, first paragraph, is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33 remain rejected under 35 U.S.C. 103(a) for being unpatentable over Palmieri et al (March 2001, Journal of Clinical Oncology, 19(5):1437-1443) in view of Scholl et al (February 2001, Cancer Research, 61:823-826) and Kuo et al (February 1998, Clinical Cancer Research, 4:411-418) for the reasons stated in the Office Action of 1/31/07, the Office Action of 9/20/07, and for the reasons set-forth below.

The claims are drawn to methods comprising detecting the mRNA expression of a panel of marker genes comprising GalNAcT and/or PAX3 in a SLN sample histopathologically negative for melanoma cells.

The Office Action of 9/20/07 contains the following text:

"Palmieri et al teaches methods of detecting metastatic melanoma cells comprising isolating nucleic acids from sentinel lymph node samples obtained from a patient, using RT-PCR to isolated nucleic acids and amplify mRNA targets from a panel of marker genes comprising MART-1 and tyrosinase (pages 1438-1439, in particular). The methods taught by Palmieri et al comprise methods wherein the sentinel lymph node samples are histopathologically negative for melanoma cells (paragraph bridging the left and right columns of page 1438), wherein the histopathology is determined by hematoxylin and eosin staining and immunohistochemistry. Palmieri et al further teaches, and one of skill in the art would recognize, that multiple-marker assays are more sensitive and specific than single-marker assays in detecting metastatic melanoma cells (page 1441 right column, in particular).

Palmieri et al does not specifically teach methods of detecting metastatic melanoma cells comprising isolating nucleic acids from sentinel lymph node samples obtained from a patient, using RT-PCR to isolated nucleic acids and amplify mRNA targets from a panel of marker genes comprising MAGE-A3, GalNAcT and/or PAX3. However, these deficiencies are made up in the teachings of Scholl et al (February 2001, Cancer Research, 61:823-826) and Kuo et al (February 1998, Clinical Cancer Research, 4:411-418).

Scholl et al teaches methods of detecting metastatic melanoma cells comprising isolating nucleic acids from a biological sample obtained from a patient, amplifying nucleic acid targets from a panel of marker genes comprising PAX3, MAGE-A3, and

tyrosinase and detecting the presence or absence of the nucleic acid targets (Table 1 and Table 2, in particular).

Kuo et al teaches methods of detecting metastatic melanoma cells comprising isolating nucleic acids from a biological sample obtained from a patient, amplifying nucleic acid targets from a panel of marker genes comprising GalNAcT and detecting the presence or absence of GalNAcT (page 413 right column, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to detect metastatic melanoma cells comprising a method of isolating nucleic acids from histopathologically negative sentinel lymph node samples obtained from a patient, using RT-PCR to isolated nucleic acids and amplify mRNA targets from a panel of marker genes comprising MART-1 and tyrosinase as taught by Palmieri et al and also amplify any other genes associated with metastatic melanoma, such as those taught by Sholl et al (PAX3 and MAGE-A3) and Kuo et al (GalNAcT). Further, one would have been motivated to do so because multiple-marker assays are more sensitive and specific than single-marker assays in detecting metastatic melanoma cells. Further, one of skill in the art would have a reasonable expectation of success in performing the claimed method since detection of genes is well known and conventional in the art."

In the Reply of 7/31/07, Applicant argues that none of the cited references disclose detection of GalNAcT or PAX3 in histopathologically negative SLN samples. Applicant further states that Examiner's assertion that there would be a reasonable expectation of success in detecting GalNAcT or PAX3 in histopathologically negative SLN samples has no basis in the cited art and there would not have been a reasonable expectation of success in detecting PAX3 or GalNacT in histopathologically negative SLN samples from melanoma patients. Applicant further argues that Palmieri, Scholl, and Kuo do not indicate that GalNAcT or PAX3 would share the same expression pattern as Tyrosinase and MART-1 simply because they are melanoma markers. Applicant further agues that it is well known in the art that not all genes are detectable in all type of samples and that a melanoma marker detected in one type of sample from a melanoma patient is not necessarily detectable in another type of sample from melanoma patients. Applicant further states that Kuo demonstrates that while GalNAcT is detectable in blood samples form AJCC stage II, III, or IV melanoma patients, it is not detectable in blood samples from AJCC stage I melanoma patients. Applicant further states that detection of PAX3 in cultured primary melanomas and their corresponding tissue sections and the detection of GalNAcT in melanoma cell lines, primary biopsies, histopathologically positive tumor-draining lymph node (TDLN) metastasis, distal organ metastasis, and blood do not indicate that GalNAcT and PAX3 would be detectable in histopathologically negative SLN samples from melanoma patients.

The arguments found in the Reply of 7/31/07 have been carefully considered, but are not deemed persuasive. In regards to the argument that none of the cited references disclose detection of GalNAcT or PAX3 in histopathologically negative SLN samples, the Examiner agrees that none of the cited references disclose detection of GalNAcT or PAX3 in histopathologically negative SLN samples. However, motivation to

detect GalNAcT and PAX3 in histopathologically negative SLN samples is discussed above. Specifically, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to detect metastatic melanoma cells comprising a method of isolating nucleic acids from both histopathologically negative and histopathologically positive sentinel lymph node samples obtained from a patient, using RT-PCR to isolated nucleic acids and amplify mRNA targets from a panel of marker genes comprising MART-1 and tyrosinase as taught by Palmieri et al and also amplify any other transcripts of genes expressed by metastatic melanoma cells, such as those taught by Sholl et al (PAX3 and MAGE-A3) and Kuo et al (GalNAcT) and one would have been motivated to do so because Palmieri et al teaches and one of skill in the art would recognize that multiple-marker assays are more sensitive and specific than single-marker assays in detecting metastatic melanoma cells.

In regards to the argument that Examiner's assertion that there would be a reasonable expectation of success in detecting GalNAcT or PAX3 in histopathologically negative SLN samples has no basis in the cited art, there would be an expectation of success in detecting levels of GalNAcT or PAX3 (both levels indicative of no transcripts and levels indicative of GalNAcT or PAX3 transcripts) because Sholl et al teaches methods of detecting levels of PAX3 transcripts and Kuo et al teaches methods of detecting levels of GalNAcT transcripts.

Further, in regards to the argument that Palmieri, Scholl, and Kuo do not indicate that GalNAcT or PAX3 would share the same expression pattern as Tyrosinase and MART-1 simply because they are melanoma markers and it is well known in the art that not all genes are detectable in all type of samples and that a melanoma marker detected in one type of sample from a melanoma patient is not necessarily detectable in another type of sample from melanoma patients, one of skill in the art would expect differential expression of GalNAcT, PAX3, Tyrosinase, and MART-1 in metastatic melanoma cells because Palmieri, Scholl, and/or Kuo teach that GalNAcT, PAX3, Tyrosinase, and MART-1 are differentially expressed in metastatic melanoma cells (note that metastatic melanoma cells are a single type of sample)."

In the Submission of 10/31/07, Applicant states that it is Applicant's discovery that GalNAcT and PAX3 are expressed in histopathologically negative SLN samples from melanoma patients. Applicant further states that without such knowledge, one skilled in the art would not have been motivated to use GalNAcT or PAX3 as a gene marker when analyzing histopathologically negative SLN samples from melanoma patients. Applicant further states that since none of the three cited references disclose

detection of GalNAcT or PAX3 in histopathologically negative SLN samples from melanoma patients, one skilled in the art would not have reasonably expected that mRNA transcripts encoded by GalNAcT and PAX3 can be detected in histopathologically negative SLN samples from melanoma patients.

The arguments found in the Submission of 10/31/07 have been carefully considered, but are not deemed persuasive. In regards to statements that it is Applicant's discovery that GalNAcT and PAX3 are expressed in histopathologically negative SLN samples from melanoma patients, methods comprising detecting GalNAcT and PAX3 in histopathologically negative SLN samples from a melanoma patient are anticipated by the *combined* teachings cited above. For example, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to diagnose metastatic melanoma by detecting melanoma cells comprising a method of isolating nucleic acids from both histopathologically negative and histopathologically positive SLN samples obtained from a patient, using RT-PCR on isolated nucleic acids and amplifying mRNA targets from a panel of genes comprising MART-1 and tyrosinase as taught by Palmieri et al and also amplify any other transcripts of genes known to be expressed by metastatic melanoma cells, such as those taught by Sholl et al (PAX3 and MAGE-A3) and Kuo et al (GalNAcT), and one would have been motivated to do so because Palmieri et al teaches, and one of skill in the art would recognize, that multiple-marker assays are more sensitive and specific as compared to single-marker assays in detecting metastatic melanoma cells for diagnosing metastatic melanoma.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 10, and 31-34 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 11/227575 for the reasons stated in the Office Action of 9/20/07.

In the Submission of 10/31/07, Applicant indicated that an appropriate terminal disclaimer would be provided if the pending claims are found to be otherwise allowable except for this ground of rejection.

Summary

Claims 31-33 are rejected under 25 U.S.C. 103(a) and all pending claims are provisionally rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA